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Title:

Quantification of drug-related toxicity associated with the prescribing of inappropriate medicines for patients with limited life expectancy.

Abstract:**Focal points**

1. Polypharmacy is common amongst patients with limited life expectancy;
2. Prescribing of inappropriate medicines for patients with limited life expectancy can lead to multiple drug interactions of varying severity;
3. Patients with limited life expectancy should have their medicines reviewed in line with the original therapeutic goals.

Background

For patients with limited life expectancy – typically surviving for less than one year from diagnosis – polypharmacy is common as medication is prescribed to manage both life limiting illness and to treat or prevent other long-term conditions. Consequently, there is an increased risk of developing drug-related toxicity resulting from drug-drug or drug-disease interactions. The aim of this work was to assess the prevalence of inappropriate medication and identify any potential theoretical drug-drug interactions in patients attending a specialist palliative care unit.

Methods

This was a prospective study that examined medication and medical histories for patients attending a specialist palliative care day care centre from November 2012 until March 2013. Medication was assessed for appropriateness using a conceptual framework, which considers remaining life expectancy of the patient, time until benefit of the treatment, goals of care and treatment targets.¹ Consensus was reached via Delphi methodology using a range of clinical pharmacists and consultants in palliative medicine; to reach consensus agreement was required from all panel members. Drug interactions were identified and assessed according to significance using the drug interaction recognition software, Proscript®. Drug interactions identified as significant were further sub-classified as moderate or severe based upon the potential to cause harm or hospitalisation, if they were reversible or irreversible and, if any treatment would be required to manage the outcome.

Results

A total of 132 patients were assessed during the study period, 108 (82%) had cancer, 8 (6%) congestive heart failure, 11 (8%) severe chronic obstructive pulmonary disease and 5 (4%) Parkinson's disease. In total, the number of medications taken was 1532 (mean per patient, 12; range 1 to 21). Of the 1532 medicines assessed, 238 (16%) were considered to be inappropriate given the patients limited life expectancy. Out of the 132 patients assessed, 92 (70%) were taking at least one inappropriate medication. The most common therapeutic group considered inappropriate were the statins, which were prescribed in 35 patients (27%). The drug interaction recognition software identified a total of 267 potential drug interactions: 155 were considered non-significant, while 112 were classified as significant. Among those identified as significant, 92 were considered moderate while 20 were considered severe. In our study, discontinuing inappropriate medicine would prevent 57 non-significant, 23 moderate and 8 severe potential drug interactions. The most frequent major potential drug interaction that could be prevented by discontinuing inappropriate medication was between simvastatin (> 20 mg daily) and amlodipine, a well-defined drug interaction, which increases the risk of myopathy; this was identified in 4 patients.

Discussion

Our results show that the majority of people accessing the day care centre in a specialist palliative care unit are being prescribed many inappropriate medications in view of their life limiting illness. These inappropriate medications contribute to potential drug interactions and thereby increase the risk of patients developing drug-related toxicity. Our findings are consistent with the literature and build upon our previous work that showed patients with advanced lung cancer take many inappropriate medications, some of which can potentially interact with chemotherapy and contribute to negative outcomes for patients.² In conclusion, these findings demonstrate there is potential for pharmacists to become involved in medication review for patients with limited life expectancy in order to facilitate discontinuation of inappropriate medication in the context of the original therapeutic goals.

References

1. Holmes HM, Hayley DC, Alexander GC *et al.* Reconsidering medication appropriateness for patients late in life. *Archives of Internal Medicine*. 2006, **166**, 605-9.
2. Todd A, Williamson S, Husband A, *et al.* Patients with advanced lung cancer: is there scope to discontinue inappropriate medication? *International Journal of Clinical Pharmacy*. 2013, **35**, 181-4